Original Article

Occurrence Of Nephrotic Syndrome In A Child Post Covid

Dr. Preethi JD [1*], Dr. N. Harsha Vardhini [2], Dr. S. Subash [3].

[1*]Post graduate, Department of Pediatrics, SRM Medical College Hospital and Research Centre, SRM Institute of Science and Technology, SRM Nagar, Kattankulathur, Kanchipuram, Chennai, Tamil Nadu, India.

[2]Assistant Professor, SRM Medical College Hospital and Research Centre, SRM Institute of Science and Technology, SRM Nagar, Kattankulathur, Kanchipuram, Chennai, Tamil Nadu, India.

[3]Professor, Head of the Department, SRM Medical College Hospital and Research Centre, SRM Institute of Science and Technology, SRM Nagar, Kattankulathur, Kanchipuram, Chennai, Tamil Nadu, India.

[*]**Corresponding Author:** Dr. PREETHI JD

[1*]Post graduate, Department of Pediatrics, SRM Medical College Hospital and Research Centre, SRM Institute of Science and Technology, SRM Nagar, Kattankulathur, Kanchipuram, Chennai, Tamil Nadu, India.

EMAIL ID: preethidas1996@gmail.com

MOBILE NUMBER: 9600064739

Doi: 10.47750/pnr.2022.13.S05.256

Abstract

Background: The incidence of COVID infection is low in children when compared in adults, and predominantly causes respiratory symptoms yet unusual cases have been reported.

Case: Presenting a girl, 6 years of age with features of nephrotic syndrome about a month after contracting a mild upper respiratory tract illness, tested positive for COVID-19 IgG antibodies, with no antecedent kidney disease.

Conclusions: The child who presented with clinical features of Nephrotic syndrome had Anti-IgG antibodies for Sars Cov2 infection. Some articles have shown proven association with the occurrence of nephrotic/ nephritic syndrome in adults either during or post Covid 19 infection. There have been similar cases of first episode Nephrotic syndrome reported post COVID infection in children. But the numbers have not been large enough to establish any association. Whether this is just a coincidence or an established sequel of COVID-19 infection is still unknown.

Keywords: SARS COV2 infection, Anasarca, Renal involvement in SARS COV2 infection, SARS-COV-2, Proteinuria, post-SARS COV-2 syndrome.

BACKGROUND:

In 2019, the pandemic due to COVID infections posed a serious challenge to Health care professionals in the world, which included challenges in the field of diagnosis treatment, and even manpower. During the onset of pandemic, children remained asymptomatic with minimal symptoms predominantly involving the respiratory system ; following which there was multi-organ involvement .[1, 2] With regards to viral tropism, especially in severely affected patients, the kidneys may also be affected, in addition to the lungs, which are the most commonly targeted organs in SARS-CoV2 infections.[3] COVID-19 infection seems to be less- frequent among children, compared to adults, with the predominant organ involved being the respiratory system .[1, 4] Incidence of Kawasaki-disease like illness and GIT syndrome have been reported in the literature,[1,2,5] yet the probability is low. Knowledge about the varied phenotypes, diagnostic challenges and treatment protocols in Nephropathies following COVID infection is minimal. In Spain, case-series containing 16 patients with End-stage renal disease with Upper and Lower Respiratory tract infections with findings in radio-imaging have been reported. Among them,

3 patients had reduced Glomerular-Filtration-Rate and 2 patients who were known case- of steroid-dependent nephrotic syndrome was diagnosed with a relapse.[6] Predominant renal involvement during the acute episode of COVID-19 is documented in the literature such as hematuria in a child[7] and hematuria with albuminuria in critically-ill children, pointing to nephritic changes in glomerulus.[8] Renal biopsy done in post-mortem samples following COVID-19 infections revealed a Nephritis-like picture indicating renal involvement. [9] Herein, we describe a pediatric patient who presented with a picture of first-episode Nephrotic syndrome, who had previously SARS CoV2 infection.

CASE:

A 6-year-old girl presented with generalized edema that started as facial puffiness progressing over a week. She was found to have anasarca with vulval edema and elevated blood pressure. Her blood and urine investigations were suggestive of nephrotic syndrome. She also tested positive for COVID-19 IgG antibodies, while COVID RT-PCR came as negative. Her antecedent history was uneventful except for an episode of respiratory tract infection (fever, coryza, cold, and cough) about a month earlier and was not evaluated for the same.

On admission: Wt.: 21.30 kilograms, Ht.: 107 centi-meters, BP: 100/60 milli-meters mercury (normotensive), Urinary analysis: 3 + proteinuria , RBCs : Nil, Hemoglobulin : 11.6 grams/dl, Hematocrit: 33%, T. protein: 4.1 mg%, serum albumin: 1.9 mg%, White Blood count: 11,780/mm^3, platelets: 3,64.000/mm^3, Na+: 137, Cl−: 114, K+: 4.8, serum creatinine: 0.5 mg/dL, HCO3: 21 meq/L, alkaline phosphatase: 188, triglycerides: 262 mg/dL, cholesterol: 309 mg/dL, RT-PCR for SARS-CoV-2 infection: negative, COVID 19 IgG antibodies: positive. C3: 187 mg/dL (RV: 90–180). Her lab investigations were suggestive of nephrotic range proteinuria with evidence of past COVID-19 infection, the rest of the parameters evaluated including C3 were within normal limits. She was managed with oral steroids (prednisolone), diuretics (furosemide, spironolactone), antihypertensives (nifedipine, amlodipine), and supportive medications for which she is showing response currently. Hence renal biopsy was done which showed a focal segmental glomerulosclerosis picture, following which she was started on immunosuppressants. She is currently stable with the above management.

DISCUSSION:

Post infections involving the respiratory system with viral etiology, like adeno-virus, influenza- A and B, renal injury has been described. Similarly, children with severe manifestations of Sars-Cov-2 infections, renal-injury is the major manifestation which includes a varied phenotypes from micro-hematuria, isolated proteinuria, azotemia, and severe acute kidney injury. [3, 7] However, after multiple reviews by the researchers, and with the current data available, isolated first-episode Nephrotic syndrome in children following COVID-19 is lacking in the literature. There are only cases that have been reported with relapses of Nephrotic syndrome post-Sars-Cov2 infection.

A systematic review was conducted in adult patients with the incidence of Nephrotic syndrome following Covid-19 or post Covid-19 vaccination in December 2021 where they included thirty-two articles, involving individual case reports and series, they observed an association with the onset of nephrotic syndrome predominantly FSGS-collapsing form.[13] The process involved in renal damage following the virus infection can be due to direct insult due to the virus or immunity-mediated or could be due to secondary to systemic complications like shock, hypoxia or hypotension. [3]

A systematic review was conducted to recommend management and treatment guidelines for COVID-19 infection and Idiopathic-nephrotic syndrome where they suggested no requirement for admission and to look-for relapses in first episode nephrotic syndrome and the indication for admission and management was severe infection by Sars-cov-2 virus. [14]

Literature suggests that following COVID-19 infection suggested patients with acute respiratory distress syndrome is primarily due to raised levels of Interlukin-4 and Interlukin-10 secreted by T-helper cells and same cytokines are responsible for podocytopathy causing renal symptoms. [15,16,17]

Other hypothesis is that, involvement of multiple organs in COVID-19 infection is due to the receptor i.e., angiotensin-converting enzyme 2, through which the virus enters the host cell and replicates which is further expressed in alveolar epithelium, myocardium , epithelium of GIT and other organs.[10]

Drugs like chloroquine or Hydroxy-chloroquine is proved in inhibiting the viral entry, thus reducing the release of

inflammatory-cytokines, yet no studies have proved the benefits of the same.[18,19]

The disease caused by Sars-cov2 infection is known to cause less severe forms in pediatric age group in comparison with adults excluding MIS-C, and the reason behind the same is that there are a smaller number of sars-cov2 targeted-receptors in pediatric age group.[6] Until today, the number of pediatric cases with acute renal involvement following sars-cov2 infection is relatively low.[5]

To summarize, this child who is being reported here was apparently healthy with no history suggestive of renal involvement ,was hospitalized due to nephrotic syndrome, tested positive for COVID-19 antibodies. There have been cases of nephrotic syndrome reported in past COVID-19 infections in the children.[11,12] Whether this is just a coincidence or an established sequel of COVID-19 infection is still unknown. However, Child specialists has to be informed and updated regarding the new-onset of complications following sars-cov2 infections in pediatric age group and to evaluate idiopathic new-onset nephrotic syndrome for Anti-Sars-cov2 antibodies.

REFERENCES:

1. Chao JY, Derespina KR, Herold BC, Goldman DL, Aldrich M, Weingarten J, Ushay HM, Cabana MD, Medar SS. Clinical characteristics and outcomes of hospitalized and critically ill children and adolescents with coronavirus disease 2019 at a tertiary care medical center in New York City. The Journal of Pediatrics. 2020 Aug 1;223:14-9.
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet. 2020 Feb 15;395(10223):497-506.
3. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, Li J, Yao Y, Ge S, Xu G. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney international. 2020 May 1;97(5):829-38.
4. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, Rovida F, Baldanti F, Marseglia GL. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. JAMA pediatrics. 2020 Sep 1;174(9):882-9.
5. Safadi MA. The intriguing features of COVID-19 in children and its impact on the pandemic.
6. Melgosa M, Madrid A, Alvárez O, Lumbreras J, Nieto F, Parada E, Perez-Beltrán V, Spanish Pediatric Nephrology Association (2020) SARS-CoV-2 infection in Spanish children with chronic kidney pathologies. Pediatr Nephrol. https://doi.org/10.1007/s00467-02004597-1.
7. Almeida FJ, Olmos RD, Oliveira DB, Monteiro CO, Thomazelli LM, Durigon EL, Sáfadi MAP (2020) Hematuria associated with SARS-CoV-2 infection in a child. Pediatr Infect Dis J 39:e161. https://doi.org/10.1097/INF.0000000000002737.
8. Gross O, Moerer O, Weber M, Huber TB, Scheithauer S. COVID-19-associated nephritis: early warning for disease severity and complications? The Lancet. 2020 May 16;395(10236):e87-8.
9. Su H, Yang M, Wan C, Yi LX, Tang F, Zhu HY, Yi F, Yang H, Fogo AB, Nie X, Zhang C. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China [published online ahead of print Apr 9, 2020]. Kidney International doi.;10.
10. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis GV, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland. 2004 Jun;203(2):631-7.
11. Sharma Y, Nasr SH, Larsen CP, Kemper A, Ormsby AH, Williamson SR. COVID-19–associated collapsing focal segmental glomerulosclerosis: a report of 2 cases. Kidney medicine. 2020 Jul 1;2(4):493-7.
12. Magoon S, Bichu P, Malhotra V, Alhashimi F, Hu Y, Khanna S, Berhanu K. COVID-19–Related glomerulopathy: a report of 2 cases of collapsing focal segmental glomerulosclerosis. Kidney medicine. 2020 Jul 1;2(4):488-92.
13. Cancarevic I, Nassar M, Medina L, Sanchez A, Parikh A, Hosna A, Devanabanda B, Vest M, Ayotunde F, Ghallab M, Omran I. Nephrotic Syndrome in Adult Patients With COVID-19 Infection or Post COVID-19 Vaccine: A Systematic Review. Cureus. 2022 Sep 26;14(9).
14. Morello W, Vianello FA, Proverbio E, Peruzzi L, Pasini A, Montini G. COVID-19 and idiopathic nephrotic syndrome in children: systematic review of the literature and recommendations from a highly affected area. Pediatric Nephrology. 2021 Oct 23:1-8.
15. Ye Q, Wang B, Mao J. Cytokine storm in COVID-19 and treatment. J Infect. 2020;80(6):607-13.
16. Chen L, Liu HG, Liu W. Analysis of clinical characteristics of 29 cases of 2019-nCoV pneumonia. Chinese Journal of Tuberculosis and respiration. 2020:1001-0939.
17. Gupta RK, Bhargava R, Shaukat AA, Albert E, Leggat J. Spectrum of podocytopathies in new-onset nephrotic syndrome following COVID-19 disease:

a report of 2 cases. BMC nephrology. 2020 Dec;21(1):1-7.

18. Tang W, Cao Z, Han M, Wang Z, Chen J, Sun W, Wu Y, Xiao W, Liu S, Chen E, Chen W. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial. bmj. 2020 May 14;369.
19. Migliaccio MG, Di Mauro M, Ricciolino R, Spiniello G, Carfora V, Verde N, Mottola FF, Coppola N, Vanvitelli COVID-19 Group. Renal involvement in COVID-19: a review of the literature. Infection and Drug Resistance. 2021 Mar 5:895-903.